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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHERNYSHEV, OLGA N	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/021,571	CHAO ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal matters

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

2. Claims 1-7 are pending and under examination in the instant office action.

2. Upon further consideration, new ground(s) of rejection are set forth as follows.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-7 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial credible asserted utility or a well-established utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

It is clear from the instant application that the protein described therein is what is termed an "orphan protein" in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken,

Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to an isolated protein of as yet undetermined function or biological significance. The instant specification states that the instant claimed protein is "a transmembrane protein which is a downstream target of neurotrophin and ephrin receptors for phosphorylation" (bottom at p. 1). The specification further discloses that neurotrophins and ephrins are related to the process of formation of the nervous system (pp. 2-4). The instant polypeptides of SEQ ID NO: 2 (rat) and SEQ ID NO: 4 (human), designated ARMS proteins (p. 15), are described as being associated "with TrkA and p75 neurotrophin receptors, a target for phosphorylation by neurotrophin and ephrin receptor tyrosin kinases, enhance[s] neurotransmitter release, and modulate[s] the clustering of proteins involved in ion channel formation" (p. 5 of the specification). Both proteins of SEQ ID NO: 2 and SEQ ID NO: 4 are

reported as being highly expressed in vertebrate central and peripheral nervous system, p. 5 and Figures 4-7, 17-18. Figures 8 and 9 show the results of the study of the interaction and colocalization of ARMS proteins and TrkA and p75. Figures 10-14 show ARMS tyrosine phosphorylation under different experimental conditions, and Figures 15 and 19-20 show interaction between ARMS and other proteins. The instant specification does not provide disclosure or explanation of the biological function of ARMS proteins of SEQ ID NO: 2 and 4, or their fragments or functional derivatives, or their significance as substrates for neurotrophin and ephrin receptor kinases for a specific physiological process or clinical condition.

In the absence of knowledge of the biological role of these specific ARMS proteins of SEQ ID NO:2 and SEQ ID NO: 4, which would support their practical utility, there appears to be no immediately obvious patentable use for the claimed polypeptides. According to the specification of the instant application "ARMS is a useful indicator of the biological activity of neurotrophins and ephrins. [...] Neurotropins and ephrins are likely candidates in spinal cord regeneration [...], and the present inventors believe that ARMS is also utilized in this process" (pp. 16-17 of the instant specification). The instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that the instant ARMS proteins of SEQ ID NO: 2 and SEQ ID NO: 4 are associated with any diseases or disorders, or would be useful for regeneration process, as asserted. To employ the proteins of the instant invention in the future methods of egulation of neuronal activity or production of antibodies is not a "real world" because it would eventually relate to a protein for which no biological function is known. The instant application also fails to demonstrate use of the proteins as markers for any disease or condition (which would be a real world use). Because the instant specification does not teach a

biological activity of the ARMS proteins, which supports their practical utility, one would not reasonably believe that the ARMS proteins can be used as markers "for neuronal cells which have the ability to undergo continued synaptic changes through adult life", as implied by the specification (pp. 26-27). To employ the proteins of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the encoded proteins in their currently available form, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-7 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Claims 1 and 4-7 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 4-7 are directed to polypeptides, which are fragments and functional derivatives of the polypeptide with a particular disclosed sequence. The claims do not require that the polypeptide possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity or by virtue of the currently not disclosed functional similarity. However, the instant specification fails to describe the entire genus of proteins, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of nucleic acid molecules which encode proteins of the amino acid sequence of SEQ ID NO: 2 (rat ARMS protein) or SEQ ID NO: 4 (human ARMS protein). The claims, however, are drawn to proteins, which are fragments and functional derivatives of the polypeptides of SEQ ID NO: 2 or SEQ ID NO: 4, and having certain functional characteristics attributes specifically to ARMS proteins. Thus, the claims are not limited to proteins with specific amino acid sequences. The claims only require the claimed polypeptides to share some degree of structural similarity to the isolated protein of SEQ ID NO: 2 or of SEQ ID NO: 4. The specification only describes a protein having the amino acid sequence of SEQ ID NO: 2 and a protein of SEQ ID NO: 4 and fails to teach or describe any other protein which lacks these amino acid sequences and has the activities possessed by the ARMS protein, such activities would include association with TrkA and p75 neurotrophin receptors, being a target for phosphorylation by neurotrophin and ephrin receptor tyrosine kinases, being able to enhance neurotransmitter release and modulate the clustering of proteins involved in ion channel formation.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of a "fragment" or a "functional derivative". There is not even identification of any particular portion of the structure that must be conserved. As stated above, it is not even clear what region of the encoded polypeptide has the biological activity and what is the specific activity of ARMS proteins, see reasoning earlier in the instant office action. The specification does not provide a complete structure of those polypeptides, which are fragments and functional derivatives of the polypeptide of SEQ ID NO: 2 or SEQ ID NO: 4 and fails to provide a representative number of species for the claimed genus. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method

of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 2 and SEQ ID NO: 4, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 1 is vague and ambiguous for recitation "wherein said fragments (C) and (D) and said function derivatives or salt (E) have the properties of associating with TrkA and p75 neurotrophin receptors [...] in ion channel formation". Specifically, claim 1 encompasses "an isolated polypeptide, which associates with TrkA and p75 neurotrophin receptors [...] involved

in ion channel formation", wherein the polypeptide has the structure recited in (A) to (E). It is not obvious what is intended by reciting the functional characteristics of the polypeptides of sections (C) to (E) twice within the claim. Clarification is required.

12. Claim 1 is further vague and indefinite for recitation "functional derivative being a chemical derivative that is derivatized at functional groups". The metes and bounds of the recitation cannot be apprehended from the claim and, therefore, the structure of the claimed molecular embodiments is no obvious.

13. Claims 5 and 7 are indefinite for "fragment (C) either further contains one or more transmembrane domains". The metes and bounds of the recitation cannot be determined from the claims or the instant specification, as filed. It appears that a fragment can only contain what is within the fragment or it can be fused with other fragments (domains) to become a fusion protein.

15. Claims 2, 3, 4 and 6 are indefinite for being dependent from indefinite claims.

Conclusion

16. No clam is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1649

May 9, 2007